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(54) **Compounds and methods associated with differential methylation of human papilloma virus genomes in epithelial cells**

(57) The invention relates to compounds and methods useful in detection and therapy of HPV-associated diseases. The invention is based on the elucidation of a mechanism by which replication of HPVs occurs in naturally infected tissues and cells. Moreover it is based on the identification of distinct epigenetic changes of the viral genome in infected cells that allows promotion of the af-

ected cells to precancerous and cancerous cells. The invention therefore provides methods of diagnosing neoplasias and their precursor lesions as well as methods of preventing the development of malignancies or inhibiting tumor growth.

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EUROPEAN SEARCH REPORT

Application Number
EP 11 17 2852

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 00/33832 A1 (GYN GENE BIOTECH CO LTD [KR]; MITSUI NORIN KK [JP]; LEE INSU [KR]; AHN) 15 June 2000 (2000-06-15) * the whole document *	1	INV. A61K31/7068 A61K31/166 A61K31/245 A61K31/353 A61K31/502 A61K31/706 A61P31/20 A61P35/00
X	CA 2 039 643 C (STIEFEL LABORATOIRES (US)) 8 November 1991 (1991-11-08) * the whole document *	1	
X,P	WO 2008/024844 A2 (UNIV JOHNS HOPKINS [US]; WU TZYY-CHOUU [US]; HUNG CHIEN-FU [US]) 28 February 2008 (2008-02-28)	4-9	
Y,P	* page 1, line 14 - line 29 * * page 2, lines 25-32 * * page 10, lines 5-9 * * page 50, lines 22-27 * * page 51, lines 15-29 * * page 67, lines 1-4 * * page 91, line 20 - page 92, line 9 * * page 93, lines 7-16 * * page 94, lines 24-29 * * figure 31 * * claims 1-8 *	2,3,10	
X,P	WO 2008/027049 A1 (UNIV TEMPLE [US]; SINAI SCHOOL MEDICINE [US]; REDDY E PREMKUMAR [US];) 6 March 2008 (2008-03-06)	4-9	
Y,P	* sentences 17-26 * * page 14, lines 6-14 * * page 25, line 5 - page 28, line 2 *	2,3,10	
		-/--	
----- -The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		9 February 2012	Bazzanini, Rita
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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EPO FORM 1503 03.82 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 11 17 2852

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	NIWA KENJI ET AL: "Topical vidarabine or 5-fluorouracil treatment against persistent HPV in genital (pre)cancerous lesions.", September 2003 (2003-09), ONCOLOGY REPORTS, VOL. 10, NR. 5, PAGE(S) 1437-1441, XP008148543, ISSN: 1021-335X * the whole document * -----	2,3,10	
			TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 9 February 2012	Examiner Bazzanini, Rita
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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EPO FORM 1503 03/82 (P04C01)



Application Number

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-10(partially)

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number

EP 11 17 2852

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-10(partially)

A demethylating agent selected from 5-azacytidine, 5-aza-2'-deoxycytidine, arabinosyl-5-azacytidine, 5,6-dihydro-5-azacytidine for use as a medicament for topical application for the treatment of HPV related lesions.

2. claims: 1-10(partially)

A demethylating agent selected from 5-fluoro-2'-deoxycytidine for use as a medicament for topical application for the treatment of HPV related lesions.

3. claims: 1-10(partially)

A demethylating agent selected from epigallocatechin-3-gallate for use as a medicament for topical application for the treatment of HPV related lesions.

4. claims: 1-10(partially)

A demethylating agent selected from hydralazine for use as a medicament for topical application for the treatment of HPV related lesions.

5. claims: 1-10(partially)

A demethylating agent selected from procainamide for use as a medicament for topical application for the treatment of HPV related lesions.

6. claims: 1-10(partially)

A demethylating agent selected from procaine for use as a medicament for topical application for the treatment of HPV related lesions.

7. claims: 1-10(partially)

A demethylating agent selected from zebularine for use as a medicament for topical application for the treatment of HPV related lesions.



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number

EP 11 17 2852

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-02-2012

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0033832 A1	15-06-2000	AU 6371599 A	26-06-2000
		KR 20000038352 A	05-07-2000
		WO 0033832 A1	15-06-2000
CA 2039643 C	08-11-1991	NONE	
WO 2008024844 A2	28-02-2008	US 2010330105 A1	30-12-2010
		WO 2008024844 A2	28-02-2008
WO 2008027049 A1	06-03-2008	CA 2661983 A1	06-03-2008
		JP 2010502602 A	28-01-2010
		US 2010305059 A1	02-12-2010
		WO 2008027049 A1	06-03-2008